Genomics Research in Africa: Implications for Disease Diagnosis, Treatment and Drug Development

Proceedings of the 5th Annual Meeting of the African Society of Human Genetics

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Abstract

This paper presents the proceedings of the 5th Annual Meeting of the African Society of Human Genetics, which took place in Cairo, Egypt, on 3rd-5th November 2007. The meeting provided a much needed forum for the development of research networks and collaborations for all who are interested in the field of 'genetics in Africa' in its broadest sense. The meeting also presented an opportunity for the Society to debate the major issues in the field and to develop a long term strategy towards achieving the goals of the Society. The most exciting and ambitious outcome of the meeting was the launch of the African Genome Project. The meeting was held in conjunction with the First Annual Meeting of the Division of Human Genetics and Genome Research and the National Society of Human Genetics of Egypt. The conference theme was 'Genomics Research in Africa: Implications for Disease Diagnosis, Treatment and Drug Development'. Over 200 participants (including clinicians, geneticists, statisticians, bioinformaticians and social scientists) attended from 28 countries, 16 of which are in Africa.

Introduction

The African Society of Human Genetics (AfSHG) was established in 2003 to 'equip the African scientific community and policymakers with the information and practical knowledge they need to contribute to the field of genetics research and to attract global attention to the efforts of African scientists' [1]. The Society's goal is to build the capacity of African researchers and institutions and create an infrastructure that can support and sustain that capacity. AfSHG aims to provide a platform on which the wealth of information and research opportunities accumulating from genomic and genetics research can be discussed. AfSHG also aims to support the exploration of modern research methods and suggest ways in which these methods can be adapted to the special conditions in Africa. This is essential if the widening gap between Africa and the Western world in biomedical science is to be addressed and access to scientific power for developing relevant resources in Africa is realised. The Society provides a forum for scientists interested in Human Genetics in Africa in its broadest sense to meet, interact, network and collaborate. This goal has been achieved through a series of annual workshops and meetings that have been held in four different African countries to date. These activities are further advanced through its website (www.afshg.org), where a wide range of web based resources are under development.

The 5th Annual Meeting of the AfSHG was held on 3rd-5th November 2007 at the National Research Centre (NRC), Cairo, in conjunction with the First Annual Meeting of the Division of Human Genetics and Genome Research and the National Society of Human Genetics of Egypt. The conference theme was 'Genomics Research in Africa: Implications for Disease Diagnosis, Treatment and Drug Development'. Over 200 participants attended from 28 countries, 16 of which are in Africa – an increase from the 10 African countries represented in 2006 as new participants particularly from North African countries were welcomed.

Opening session and keynote address: Africa and the Genomics Revolution

The opening keynote address (Africa and the Genome Revolution was given by Professor Francis Collins, Director of the National Human Genome Research Institute, National Institutes of Health, USA. Of his many achievements, perhaps the most notable was Professor Collins' stewardship of the Human Genome Project (HGP). Professor Collins is now focused on efforts to ensure the HGP output is translated into tools and strategies to advance biological knowledge and improve human health. Professor Collins began with an overview of the achievements of the HGP and went on to outline important areas in which advances in genomics were likely to have benefits for human health. Although the main focus of his talk was the human genome, the audience was reminded that much progress has also been made in deciphering the genomic sequences of major pathogens and vectors that are responsible for millions of deaths each year, especially in African countries.

Our understanding of the genetics of common diseases has advanced rapidly since the availability of the human genome content and the International HapMap project which has provided a map of single nucleotide polymorphisms (SNPs) as well as information on linkage disequilibrium across the genome. In 2002 the genetic basis of approximately 1600 Mendelian disorders had been established, yet only seven complex trait genes had been identified [2]. The HapMap project (including the recently published phase II) [3] coupled with the technological developments it drove, has allowed genome wide association studies to become practical and affordable. This has led to an exponential discovery of genetic variants associated with common diseases in the last few years.

Specific applications of the human genome information were described. The Cancer Genome Atlas is a collaboration between the National Human Genome Research Institute and the National Cancer Institute which aims to apply genome analysis technologies to accelerate our understanding of the molecular basis of cancer. The HGP has also empowered much needed new drug discovery for neglected diseases that afflict millions of people living in resource-poor environments. Professor Collins closed by considering the

future of genome research in Africa. He highlighted the unique resources available – the great genetic diversity of African populations and their unique health problems, coupled with talent and creativity – and underlined the need for collaboration across the continent. He concluded that whilst the science of genomics is new, in the long run its implications for healthcare in Africa are highly significant.

Understanding genetic diseases in Africa: implications for research and public health strategies

Professor Dominic Kwiatkowski (UK) explained how genetic networks such as MalariaGEN (http://www.malariagen.net/) could be used to unravel factors contributing to the causes and prevention of severe malaria. He emphasized how collaborative effort was essential to achieve the objectives of MalariaGEN, which will require collection of DNA samples from more than 10,000 children with severe malaria. He also talked about issues surrounding the management and release of large volumes of genetic data, and mentioned the fellowship program in data analysis which is an important part of the network.

Professor Charles Rotimi (USA) highlighted the importance of large scale collaborations as he used the example of the African American Diabetes Mellitus study (AADM) [4] to update the audience on the effect that new technologies are having on our ability to study complex diseases. He stressed the limitations posed by the current way most environmental data are gathered, and the public health issues raised by screening affected families in situations where medication availability is not guaranteed. However, the overall picture he delivered was very positive in terms of the progress of the three phases of AADM. So far, this ongoing genetic epidemiology project has enrolled and examined over 3,500 persons with type 2 diabetes and controls from four major ethnic groups in Ghana (Akan and Gaa) and Nigeria (Ibo and Yoruba).

Professor Raj Ramesar (South Africa) presented data gathered from many years of study of families susceptible to colon cancer. He demonstrated the benefits of genetic screening not just on more precise targeting of colonoscopic screening, but also on overall mortality. He gave a thoughtful community perspective on screening for colon cancer, illustrating the need to move screening out to the community, and to study which factors affect uptake of information and attendance for screening.

The experience of the African Diaspora was used by Dr Adebowale Adeyemo to discuss different approaches (genome wide scans, candidate gene studies, and others) to the genetics of hypertension. He summarized the candidate gene approach, pointing out the many inconsistencies that have arisen to date, the lack of replication and the problems of associations being found with intermediate phenotypes but not with hypertension itself. He described a couple of studies that used the admixture mapping approach, noting the utility of such study designs in populations such as African Americans. He noted a lack of African studies in meta-analyses of genome-wide scans for hypertension. He concluded by highlighting the need for more studies of the genetics of hypertension in African populations and for inclusion of African populations in genome wide association studies.

Dr Donald Coppock (USA) and Professor Duncan Ngare (Kenya) talked about practical issues relating to setting up International HapMap Repositories. Dr Coppock concentrated on quality and safety issues at the Coriell Repository, and the importance of regular feedback to participating communities through newsletters. Professor Ngare focused on issues of information and consent that had arisen during data collection among the Masaai population in Kenya.

Understanding the genetic basis of common diseases

Professor Samia Temtamy (Egypt) gave an overview of the genetics of limb and skeletal malformations, one of the most important causes of disability in Egypt (prevalence rate of

1.7/1000). She concluded that with the recent advances in molecular medicine it is becoming mandatory to apply these techniques in order to facilitate better understanding of the pathogenesis and genetics of these conditions. Professors Riad Bayoumi and Mohammed Hassan (Oman) described their efforts to identify loci underlying obesity/diabetes and hypertension respectively in the 'Oman Family Study'. Five large extended consanguineous Arab families comprising 1280 persons have been phenotyped in great detail and genome wide linkage studies conducted in order to identify genes linked to various metabolic phenotypes. A number of novel loci detected through these studies are under further investigation.

Human genetic variation and disease

An update on 'Human polymorphisms and malaria selection' by Professor Lucio Luzzatto (Italy) combined clinical work with recent molecular advances in malaria. His talk started by reminding the audience of the role of natural selection in shaping genomes in their response to changes in the environment. He then reviewed the pathogenesis of malaria disease, describing the intimate relationship between the parasite and host in the pathophysiology of malaria. There have been different types of genetic adaptations in malaria: (1) those that affect the intracellular parasite in the vertebrate host, (2) powerful selection in one generation, and (3) consistent selection over some 300 years. Several genes in the human host have been implicated in resistance or susceptibility to malaria (α-globin, β-globin, spectrin, erythrocyte band 3, glycophorin C, G6PD, HLA-B, HLA-DBR1, TNF, CD36, ABO blood groups, Duffy chemokine receptor, ICAM-1, Complement receptor-1).

Professor Luzzatto discussed the epidemiology of α- & β-globin polymorphisms, focusing on the β-globin-S (sickle) polymorphism, haemoglobin C, and then the role of glucose-6-phospate dehydrogenase (G6PD) deficiency in malaria. According to Professor Luzzatto, malaria is a tale of three genomes: (1) adaptive changes in the parasite, (2) adaptive changes in the vector and (3) adaptive changes in the human. His presentation

contextualized these components and highlighted how the effects of selection and genetic drift influenced population dynamics.

Dr Floyd Reed (USA), spoke on the genetic basis of human adaptation in Africa and its implications for human evolution and human disease. Numerous microsatellite and insertion-deletion polymorphisms were genotyped in 84 African ethnic groups, as well as samples drawn from African American, Yemeni, Indian, Caucasian, and Australian populations, and patterns of variation analyzed using the STRUCTURE program. There was evidence for partitioning of the data between African and non-African populations, and as the numbers of cluster groups increased, there was a concomitant partitioning within the African region showing that the populations presently in residence in West, East, North, Central and Southern Africa harbor very distinctive collective patterns of variation. However, while the program STRUCTURE was good at dividing individuals into clusters that represented recent population structure, it could not directly provide information on the evolutionary history of the populations. The isolation with migration method [5] was thus used to jointly infer the amount of migration and time of common ancestry between pairs of populations. Interestingly, Southern Africa showed the highest amount of genetic structure (layers of different patterns of variation) followed by the Middle Eastern Area and then East Africa.

Dr Sylvester Kajuna (Tanzania) spoke on 'Genetic diversity within Africa based on autosomal haplotypes'. The objective of this research was to establish a large set of markers on African populations that could serve three purposes: (1) determine the genetic relationships of African populations in the global context, (2) serve as a reference set of markers for future studies, and (3) examine the value of haplotypes for defining and understanding the relationships among African populations and the effects of "Out of Africa" founder effects. The sample of African populations consisted of Biaka from Central African Republic; Mbuti from the Democratic Republic of Congo; Yoruba, Ibo and Hausa from

Nigeria; and Masai, Chagga and Sandawe from Tanzania. Other populations sampled included Ethiopian Jews, African Americans, SW Asians/Europeans, and San , Mandenka, Bantu-speakers and Mozabites from the HGDP-CEPH sample collection. Analysis of haplotype data for two genes (*BRCA1* and *SLC6A4*) showed higher genetic variation being found among African populations compared with those outside of Africa – an observation that has been supported by many other studies.

Understanding the human journey within and outside Africa

Continuing on the theme of human population variation in Africa, Dr Himla Soodyall's (South Africa) talk entitled "Understanding human migration: the Genographic Project" focused on how mtDNA and Y chromosome DNA variation can be used to map patterns of genetic variation within sub-Saharan Africa. The Genographic Project was launched in 2005 as a multi-dimensional initiative with three major activities: (1) a global DNA sampling aimed at collecting approximately 100,000 samples from indigenous populations around the world, and to use these samples for anthropological research in an attempt to answer fundamental questions about humankind's origins and migrations, (2) a public participation component through which members of the public could purchase cheek swab kits to trace their ancestries, and (3) an educational legacy project that will benefit communities and peoples participating in the research.

Dr Soodyall presented her research under three themes. Firstly, she discussed the use of autosomal DNA SNPs in examining the genetic structure and affinities of San, Khoe and Bantu-speaking groups in southern Africa. Using the programme STRUCTURE it was clear that the San and Khoe shared a common genetic background and this background of genetic variation ranged in frequency (25-90%) among the different San and Khoe groups examined. Secondly, she discussed how trade activities in the wider Indian Ocean Rim have influenced the gene pools of African (Zanzibar) and Malagasy populations.

Approximately 95% of mtDNA types found in Zanzibar was traced to origins in Africa with the remaining 5% tracing to non-African sources, predominantly Asian. However, when Y chromosome DNA markers were used about 20% of Y chromosome could be traced to non-African geographic regions of origin, especially from the Middle East. Thirdly, she reported that mtDNA and Y chromosome DNA signatures found among African populations may still harbor vital clues concerning the geographic region of origin of modern humans. Some of the oldest surviving mtDNA and Y chromosome DNA lineages are found among people who presently self-identified as San and Khoe.

Dr Emily Neimitz (Nature Genetics, USA) closed this session with a stimulating discussion of regional populations and the increasingly flat world of genetics. Her title was inspired by a book, 'The world is flat', written by Thomas L Freidman which explores how new technologies have circumvented traditional obstacles to development as people 'plug, play, compete, connect and collaborate with more equal power than ever before'[6].

Genetics and genomics of cancer

Professor Sir Walter Bodmer introduced the main concept underpinning the molecular basis of cancer - that cancer is a somatic evolutionary process in which successive genetic mutations or changes in gene expression are selected for. The challenge is to identify these changes, to establish their functional basis and to find ways to use the information for early detection and the development of new drugs. Professor Bodmer illustrated this concept using genes involved in colorectal cancer (CRC). Although predisposition to CRC is inherited as a dominant trait, germline mutations only contribute to cancer development if there is a second somatic event leading to the loss of the single wild type allele. Mutations in genes encoding components of the Wnt pathway, cell cycle check points, growth factor signalling receptors, apoptosis and the immune system have all been associated with CRC and selection for mutations in different pathways will occur at different stages of the transition from adenoma to carcinoma.

Professor Bodmer also discussed the impact of carcinogenic mutations at the population level, addressing the 'common alleles versus rare variants' hypothesis postulated for common multifactorial diseases. In the former, disease association is detected as a result of linkage disequilibrium with a common allele and the odds ratios are generally small. In the latter, rare variants, each with a moderate effect, in a number of genes cumulatively have a larger and more readily detectable effect. Professor Bodmer elegantly addressed this dichotomy using data generated from patients with multiple adenomatous polyps (MAP) who were screened for germline variants in genes involved in wnt signalling (APC, Axin1 and CTNNB1) and mismatch repair (hMLH1 and hMSH2) on the assumption that such variants could give rise to inherited susceptibility to colorectal adenomas. 483 healthy population controls were then screened for any DNA variants identified in the MAP patients. These variants were twice as common in the MAP cases compared to controls, and the majority were functional. The odds ratios associated with the variants were high, yet the low frequency of the individual variants precludes them from being useful in classic cases control studies. In contrast, common alleles found to be associated with disease in case control studies have lower odds ratios and since they are in linkage disequilibrium with the causative variant, ascertaining function is difficult. A review of published data showed a clear reciprocal pattern between odds ratio for rare versus common variants. Reviewing data for BRCA2 and breast cancer he concluded that collectively, rare variants make a substantially greater contribution to genetic susceptibility at loci such as BRCA1, 2 and APC than the total of frankly deleterious familial mutations. Taken together, these analyses have important strategic implications for scientists aiming to identify disease genes – the currently fashionable genome wide association studies that use common SNPs to detect association will miss the important rare causative variants that can only be detected through sequencing of candidate genes in carefully selected patients.

Dr Hassan Ashktorab (USA) described studies of sporadic colorectal cancers for expression and methylation status of mismatch repair genes known to be involved in colorectal cancer

and other epigenetic phenomena such as global acetylation of histone 3 and 4 and HDAC2, and microsatellite instability. Genome wide approaches including comparative genome hybridization were also employed. A number of genetic and epigenetic changes in sporadic colorectal cancers in African Americans were identified and it was postulated that an integrative approach could help identify pathways involved in colorectal carcinogenesis.

Dr Renato Mariani-Costantini (Italy) presented his studies on breast cancer in Central Sudan, a disease that to date has been relatively neglected in Sub-Saharan Africa. BRCA1, BRCA2 and p53, the three main genes associated with breast cancer, were studied in young women presenting with breast cancer in Sudan. Through sequencing, a number of variants were identified in these genes, many of which were unique to the population. A subset of these mutations were pathological and comparison with Italian cases demonstrated that Sudanese cases tended to be younger, with more advanced, more aggressive disease that was more likely to be estrogen receptor positive in immunohistochemical staining than the Italian cases.

Professor Lofti Chouchane (Qatar) discussed the preventative and predictive medicine implications of the advances in the genomics of cancer. Professor Chouchane discussed the known germline mutations in genes such as BRCA1 and 2 that are responsible for familial forms of breast cancer. However, there are differences in patterns of disease between populations that involve other genetic factors as well as socioeconomic factors. Professor Chouchane highlighted the role of immune response genes in the development of breast cancers, with polymorphisms in pro-inflammatory genes such as interleukins 1 and 6 and tumour necrosis factor being associated with a worse prognosis for some women.

Dr Wael El-Rifae (USA) gave a concise overview of how functional integrated 'Omics' can contribute to our understanding of malignant disease. His laboratory has taken a lead in the molecular characterization of upper gastrointestinal adenocarcinomas (UGC) and in making

use of the 'omic' information from genomics, epigenomics, transcriptomics, and proteomics to better understand the cancer genome as well as the possible clinical and therapeutic impact of the findings. Comparative genomic hybridization analysis revealed a complex pattern of DNA losses and amplifications. The group has mapped the genomic and transcriptomic molecular alterations and developed an anatomical view of these genetic changes along the human genome. Clusters of transcriptional oncogenomic hotspots were identified and classification of genes into functional sets according to their biological and molecular activity revealed alterations of cellular pathways including cell cycle regulation, adhesion, apoptosis, and invasion. Some of the most clinically relevant findings of this integrated approach are the detection of alterations in several genes that are candidate therapeutic targets for UGCs.

Genomic technologies, pharmacogenomics and bioinformatics

Dr Farideh Chitsaz (USA) gave an educational overview of the facilities available to identify disease causing genes *in silico*, through genomic sequence data mining. Online resources are expanding and the facilities available though the National Center for Biotechnology Information were described. Professor Giuseppe Novelli (Italy) spoke about genomic biomarkers in pharmacogenetics and pharmacogenomics, using large clinical intervention trials for cardiovascular disease as his starting point. Whilst many patients benefit from such interventions, others do not and some have serious adverse reactions to the intervention. There is undoubtedly a genetic contribution to such responses and further studies are required to unravel which genes are involved and how they interact with environmental factors. One of the roles of the AfSHG is to promote networking, training and collaboration within the African continent. Bioinformatics lends itself well to this model as it does not require expensive technology and reagents and there are well established centres of excellence. Dr Daniel Jacobson, of the National Bioinformatics Network, South Africa, described a model for bioinformatics networks in Africa based on the system being pioneered in South Africa. Dr Pasquale De Blasio (Italy) spoke in the topic of biorepositories

in Africa. These are key resources in the days of genome and proteome based research, and whilst the advantages of setting up large collections of biological material may be obvious, there are a number of problems that need to be overcome.

Tomorrow's technologies

Dr David Bentley (Illumina Inc) played a leading role in the human genome sequencing project as well as the SNP Consortium and the International HapMap Project. He has been at the forefront of development of new DNA sequencing technologies and the subject of his talk at this meeting was "New sequencing technology and changing horizons". As well as describing the new technologies, Dr Bentley explained the applications of such advances. Whilst the human genome project was a major scientific landmark, cheaper, faster methods are required to enable wider application of genomic advances, for example to allow discovery of genetic variation underpinning disease and enhanced understanding of the biological implications (and therefore potential therapeutic interventions) of this variation. Dr Bentley also illustrated how such advances can be applied to other organisms, focusing in his talk on *Mycobacterium tuberculosis*, one of the leading infectious killers of humans.

Tomorrow's medicine

Dr Griffin Rodgers, Director of the National Institute of Diabetes, Digestive and Kidney Diseases, NIH, USA, and internationally recognised for his research towards the development of new therapies for sickle cell disease (SCD) spoke on 'Stem cell therapy for sickle cell disease: transplantation and gene therapy'. Dr Rodgers reviewed the molecular pathophysiology underlying the chronic haemolysis and microinfarction that characterises SCD. It is recognised that although all patients with SCD are homozygous for the same mutation, there is huge variation in the clinical phenotype and the factors that modify the disease phenotype include the genetic haplotype in which the sickle mutation is embedded, other genetics factors, local cellular and physiological factors and psychosocial factors. He went on to describe the discovery of hydroxyurea as a successful new therapy for SCD,

acting through increasing the level of fetal haemoglobin, but noted that this did not work for all patients. This observation drove research on stem cell therapies aimed at replacing the defective erythrocyte population. Traditional ablative methods of stem cell transplantation are being superceded by less intensive (non-myeloablative) stem cell transplantation which is now being assessed in carefully selected patients.

Dr Alice Abdel-Aleem (Egypt) described her studies on the differentiation of neuroprogenitor cells derived from human embryonic stem cells into various neuronal cell types, focusing especially on the technical challenges of this work, bringing together scientists from the fields of molecular biology, molecular genetics, biomaterials and laser technology. Dr Tarek Badry (Egypt) described the application of stem cell technology to the development of new therapies for reconstruction of tissues and bone *in vivo* using dental pulp stem cells and periodontal ligament stem cells. These cells have a number of stem cell-like properties and their easy accessibility is an added advantage.

Free papers

Two sessions of the meeting were dedicated to free oral papers selected from submitted abstracts. A wide variety of topics from a number of studies based in different locations across Africa were covered, including:

Population genetics (Hisham Hassan, Sudan; Iliena Pietrangeli, Italy/Benin/Mongolia), cytogenetic techniques (Ashraf Ibrahim, Egypt), gene expression (Yousif Idaghdour, USA/Morocco), vaccine response genetics (Dr Branwen Hennig, UK/Gambia), systematic reviews (Mark Engel, South Africa), molecular diagnosis and genetic counselling especially regarding congenital disorders (Katherine Balk, USA/Mali; Wafa Cherif, Tunisia; Wafa Troudi, Tunisia; Dr Ambroise Wonkam, Cameroon), comparative genomics (Dr Mohamed Aboueldhouda, Germany/Egypt), ethical issues (Professor Gail Davey, Ethiopia) and database establishment (Dr Ghada Abdel-Salam, Egypt).

The work presented gave a good overview of the breadth of research going on across the continent at present. It also gave a snapshot of the background and setting for many studies, whether studies were carried out fully in Africa or in collaboration with others outside of Africa. For instance, international collaborations give opportunity to some scientists to access large-scale facilities (still lacking in most parts of Africa) whilst simultaneously, researchers in the field of human genetics in Africa are shifting from simply providing samples to building and strengthening local capacities to investigate genetic diseases, particularly for hereditary monogenic diseases, which is of great importance in tackling the "genomic" divide. A total of 55 posters selected from submitted abstracts were also presented over the course of this meeting.

AfSHG Young Investigator Prize

The Young Investigator Prize was launched at this AfSHG meeting with the aim to promote young researchers in the field of genetics in African populations or those of African ancestry. A panel consisting of five judges was appointed to nominate the three best oral presentations. There were 11 entries for the best oral and 53 for the best poster presentations, from researchers based in 21 different countries. We are grateful to all sponsors who supported this Prize competition, through which the winners have gained online subscriptions to scientific journals or received text books that are often not accessible for those based in African countries, or were given sponsorship to attend the next annual meeting of the AfSHG.

Developing an African Genome Project to ensure that tomorrow's medicine and technology will work for all humans

The potential benefits of the ongoing Human Genome Project and similar genomic research are enormous and may form the basis of many breakthroughs in biomedical technology and healthcare. Furthermore, the continent of Africa has a significant attachment to the human

genome and may hold the key to our understanding of its current form and how it may change in the future. This understanding may shed light on the best ways to manipulate information about the human genome and other genomes for the benefit of individuals and society. Given its objectives, the AfSHG is well –placed to lead the development of an exciting, ambitious new initiative: the African Genome Project (AGP), and a consultation with the wider membership took place during the 5th AfSHG meeting. This consultation allowed leading African and international scientists to discuss the opportunities and challenges of developing this major African biomedical project that will support large-scale population based application of recent genomics tools to gain novel insight into the determinants of both communicable and non-communicable diseases important to Africa populations.

A major rationale for the establishment and design of an AGP was the concern that the equity gap that already exists between developed and developing countries will be widened if developing country populations, their scientists and health practitioners are not fully engaged in the application of genomic tools to address global problems including health and food production. It was also widely expressed that global inequality in health will be exacerbated if we do not ensure that "Tomorrow's Medicine and Technology" will work for all humans and that Africa will not be left out of the genomic revolution.

The AGP will define the critical research priorities required to improve health for all Africans, and the study designs required to tackle them through capturing the genetic diversity within the continent and subsequent application to disease. The AGP will foster partnerships that enhance capacity building and infrastructure development through strengthening of local expertise at the level of the continent, rather than country or institutional level.

The AGP project will have four major components: population genetics, medical genetics, training and infrastructure development. The population genetics component of AGP will facilitate a more comprehensive understanding of genetic diversity in African people by

conducting a systematic sampling a minimum of 100 ethnic groups across the continent (North, East, West, Central and South). The medical genetics aspect of AGP will facilitate the development of large-scale population based resources to understand the genetic and environmental determinants of diseases important to African people and the global community. The third component of the AGP will facilitate the training and participation of African scientists in the global effort to use genomic tools to solve global health problems. Successful implementation of the first three components of the AGP will require the development and implementation of appropriate infrastructure in strategic locations in the continent.

When the burden of disease is analyzed, it is clear where the research priorities lie: for example, HIV, malaria and TB claim millions of lives, and the increasing prevalence of non-communicable diseases such as hypertension, diabetes and mental health disorders is contributing hugely to changing disease demographics in Africa. However, whilst the health priorities may appear to be obvious, many questions remain that will inform and shape the development of the AGP: exactly who should we study; who are the stakeholders; how do we ensure engagement of African populations and their leaders for full support for the project?

Careful assessment of existing infrastructure within Africa is needed as is the identification and/or establishment of regional infrastructure that will support sample collection, processing and storage. Development of regional genomics laboratories in Africa is required to facilitate the engagement and training of African scientists and students in genomic research.

Ethical considerations in the implementation of an African Genome Project

There are several complex ethical, cultural, social and potentially legal issues to consider around the implementation of the AGP. It is likely that these issues can be satisfactorily

addressed by careful engagement of African communities, design and interpretation of study results. Three key components of the proposed project have been identified: Governance, Research, and Translation, and these need to be considered in conjunction with the three supporting and areas of education and training, community engagement, and capacity building.

Questions regarding Governance include: In which country or countries will the project be based? Who will have oversight of the resource? Where will the resource be housed? How will decision-making take place regarding the project? What are the potential funding mechanisms for such a project? Clearly, issues of representation, equity, and control and power would be crucial to future deliberations and resolution about leadership of the project.

With regard to Research, there are concerns about genetic variation research and its implications for African communities, in particular, around the potential for reification of existing notions of difference and/or the creation of new opportunities for stigmatization, discrimination, and conflict. There was unanimous agreement by the AfSHG membership that this is a valid concern that requires substantial attention and that must be carefully balanced with the potential benefit of the project to Africa and the global community. Some meeting participants also expressed fear that African investigators would not have equal access to the resource, ample opportunity to lead or collaborate on research projects, or receive adequate recognition (eg. authorship on publications) for their contributions to projects. These discussions served to highlight the exceptional role of the supporting elements (education/training, community engagement, and capacity building) in all aspects of the development of the resource and implementation of related research.

Regarding issues associated with Translation and the practical or clinical application of the research, there are questions concerning access of Africans to diagnostics, treatments, and preventive measures emanating from the research. The establishment of strategic

partnerships with biotechnology and pharmaceutical may be required to address this issue. A need was identified for deliberate attention to education and training for genetic counsellors and other genetics professionals who would interpret and communicate clinical genetics findings, as well as for clinicians who would incorporate these genetic and genomic findings into their healthcare practices. In addition, there was considerable discussion about potential personal, cultural, and social barriers to utilization of genome-related services among Africans. This led to the acknowledgement of the dearth of available information on these issues within Africa, and underscored the need for additional research in this arena.

Discussions at the annual meeting formed an extremely useful starting point for considering the potential ethical and social implications of a project of this magnitude. As ideas about an AGP continue to develop, attention to these critical underlying issues will also evolve as we seek to ensure maximum benefit and minimum harm to African individuals, families, communities, and societies.

In summary, the AGP is firmly on the agenda for the AfSHG and a special meeting to further develop the initiative, in which stakeholders and potential funding agencies will also participate, is planned for 2009 when the AfSHG next meets.

Further information about the AfSHG and its activities, including the AGP is available at www.afshg.org.

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Young Investigator Prize winners and panel

From left to right: Prof. Charles Rotimi (AfSHG president), Nejla Bel Hedi, Youssef Idaghour, Illenia Pietrangeli, Kathy Balk, Alice Matimba, Prof. Samia Temtamy (local committee, judge), Dr. Branwen Hennig (Prize coordinator), Yasmin Khalel, Prof. Sir Walter Bodmer (judge); not shown Ashraf Hosni Ibrahim, Amani A. Elamin and Shamman Sewram.